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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,105	08/15/2001	Fred S. Lamb	875.054US1	9991

53137 7590 01/03/2006

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/930,105	LAMB ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,27-29,31-35 and 38-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,27-29,31-35,38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In view of the appeal brief filed on 06 October 2005, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-24, 27-36 and 38-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "modulating vascular tone in a **specific patient population** (e.g. 35-year young man) having compromised vascular tissue, comprising administering a pharmaceutically effective amount of a

chloride channel blocking agent, wherein the compromised vascular tissue is associated with **erectile dysfunction**", does not reasonably provide enablement for the "**a patient** having compromised vascular tissue, comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, wherein the compromised vascular tissue is associated with **erectile dysfunction**". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method to modulate vascular tone in a patient having compromised vascular tissue, comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof, wherein the compromised vascular tissue is associated with erectile dysfunction. The nature of the invention is extremely complex in that it encompasses any patient such that the any subject treated with above compounds having modulated vascular tone in vascular tissue associated with erectile dysfunction.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass modulating vascular tone in any patient having compromised vascular tissue associated with erectile dysfunction in any patient which has potentially many different causes (i.e. many different disorders or combination of disorders involving medication side-effects, psychological). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to **a patient** in order to actually modulate vascular tone in a patient having compromised vascular tissue associated with erectile dysfunction is minimal. All of the guidance provided by the specification is directed towards modulating vascular tone in a **specific patient population rather than any patient.**

Working Examples: All of the working examples provided by the specification are directed toward the **specific population rather than any patient.**

State of the Art: While the state of the art is relatively high with regard to modulating vascular tone in a specific patient population (men) having compromised vascular tissue associated with **erectile dysfunction** with **tamoxifen**, the state of the art with regard to modulating vascular tone in a any patient having compromised vascular tissue associated with **erectile dysfunction** with **tamoxifen** is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound

similar to the claimed compounds was administered to a subject to modulate vascular tone in any patient population having compromised vascular tissue associated with **erectile dysfunction** with **tamoxifen. Applicant's attention is drawn to the prior art of record, Delaney et al. (1996), wherein it teach approximately 50% of women report loss of libido as a significant clinical problem. Delaney et al. report that previous studies had found that 5 to 30 percent of men receiving tamoxifen experienced reduced libido. (page 53, right-hand side last paragraph bridging to page 54). These teachings report that tamoxifen does not work to modulate vascular tone in any population of patients (including any men and women) compromised vascular tissue associated with erectile dysfunction because tamoxifen significantly causes women and men in any population to loss libido.**

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual modulation of vascular tone in **any patient** compromised vascular tissue associated with erectile dysfunction with the claimed compounds makes practicing the claimed invention unpredictable in terms of from the specification or prior art with regard to the actual modulation of vascular tone in **any patient** compromised vascular tissue associated with erectile dysfunction.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment,

route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for modulating vascular tone in **a patient** including women and any men having compromised vascular tissue, comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof, wherein the compromised vascular tissue is associated with erectile dysfunction. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to modulating vascular tone in **a patient** having compromised vascular tissue, comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof, wherein the compromised vascular tissue is associated with erectile dysfunction, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding modulating vascular tone in a patient having compromised vascular tissue, comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof, wherein the compromised vascular tissue is associated with erectile dysfunction, the entire, unpredictable

process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to a method to **modulate vascular tone in a patient having** compromised vascular tissue, comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof, wherein the compromised vascular tissue is associated with erectile dysfunction.

Therefore, a method to modulate vascular tone **in any patient having** compromised vascular tissue, comprising administering a pharmaceutically effective amount of a chloride channel blocking agent, or a pharmaceutically acceptable salt thereof, wherein the compromised vascular tissue is associated with erectile dysfunction is not considered to be enabled by the instant specification and the preponderance evidence of the supported prior art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22-24,27-29, 33-35, 39-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Delaney et al. (1996) evidenced by Kifor et al. (U.S. Patent No. 5,658,936) all of record.

Delaney et al. teach that patient treated with tamoxifen significantly enhanced libido and reported that Patient's libido has returned to normal. (under Case Report, second paragraph, under Discussion).

Applicants' recitation in claims of mechanism of action to modulate vascular tone and reduces penile sympathetic tone does not represent a patentable limitation by which tamoxifen gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects (enhance erection) which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make novel since the treatment of the conditions encompassed by the claims.

Kifor et al. report that an improvement in erectile function is defined as increased libido. (column 6, line 66- column 7, lines 9).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 31, 32 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delaney et al. (1996) as applied to claims 22-24,27-29, 33-35, 39-43 above, and further in view of Zhang et al. (U.S.Patent No. 6,266,560 B1) and Drug Facts and Comparisons, 1997 all of record.

Delaney et al. as applied as before.

Delaney et al. do not expressly teach route of administration set forth in claims 32 and 38 and further administering the agents set forth in claim 31.

Zhang et al. report that vasodilators is useful for the treatment of erectile dysfunction. (column 2, lines 6-10).

Drug Facts and Comparisons teaches tamoxifen is commercially available orally. (page 3162, bottom table under Nolvadex).

It would have been obvious to one of ordinary skill in the art to incorporate the agents (i.e. vasodilators) with tamoxifen because vasodilators are useful for the treatment of erectile dysfunction as Zhang et al. One would have been motivated to combine vasodilators with tamoxifen for the treatment of erectile dysfunction in order to achieve at least an additive effect for the treatment of erectile dysfunction. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). Moreover, the route of administration of tamoxifen is obvious since oral formulation of tamoxifen is commercially available as taught by Drug Facts and Comparisons.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicant's arguments filed October 6, 2005 have been fully considered but they are not persuasive. Applicant argues Delaney et al. fails to anticipate the present claims because Delaney et al. discloses that one male patient on a tamoxifen regimen had experienced increased libido during his course of treatment. This is not persuasive because Delaney et al. teach that one patient had experienced increased libido during his course of treatment meets Applicant's claimed limitation. Therefore, claimed subject matter is anticipated by Delaney et al. and the mechanism for modulating penile vascular tone is inherent biological pathway upon administration of same compound (tamoxifen) with same amounts to same population. Applicant argues the increase in libido observed in this one patient was contrary to other case reports in which tamoxifen therapy was associated with impotence. This is not persuasive because Delaney et al. still report that one male patient on a tamoxifen regimen had experienced increased libido during his course of treatment and the subject matter is anticipatory. Further there is enablement issue concerning claimed subject matter that there is unpredictability in Applicant's invention. Applicant argues that libido and erectile dysfunction are significantly different conditions. This is not persuasive because Kifor et al. patent defines improvement of erectile dysfunction as increase libido. Applicant further argues Zhang et al. patent and the Drug Facts and Comparisons document fail to remedy the deficiencies of Delaney et al. because either of these documents suggest that a chloride channel blocking agent such as tamoxifen would be useful either to modulate vascular tone in the patent having compromised vascular tissue associated with erectile dysfunction or to modulate penile vascular tone in a mammal in need

thereof. This is not persuasive because Zhang et al. report that vasodilators are useful for the treatment of erectile dysfunction and Drug Facts and Comparison teaches tamoxifen is commercially available orally. Therefore, these teachings obviate the limitation claimed by the Applicants' in claims 31, 32 and 38. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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December 23, 2005

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